(FILE 'HOME' ENTERED AT 15:37:43 ON 30 MAY 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 15:38:00 ON 30 MAY 2002

L1	733	S PLUCKTHUN A?/AU OR NIEBA L?/AU OR HONEGGER A?/AU
L2	355	S L1 AND ANTIBOD?
L3	2	S L2 AND HYDROPHILIC
L4	29	S L2 AND INTERFACE
L5	2	S L3 AND L4
L6	29	S L3 OR L4
L7	7	S L4 AND SOLUBIL?
L8	6	S L7 NOT L5
L9	3	DUP REM L8 (3 DUPLICATES REMOVED)
L10	28	S ANTIBOD? (P) HYDROPH? (P) INTERFACE? (P) SOLUB?
L11	11	DUP REM L10 (17 DUPLICATES REMOVED)
L12	9	S L11 NOT L6

WEST Search History

DATE: Thursday, May 30, 2002

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR		
L4	antibod$4 same interface$4 same hydroph$4 same solubil$4	3	L4
L3	L2 and antibod$4	12	L3
L2	(pluckthun)[IN] OR (nieba)[IN] or (honegger)[in]	388	L2
L1	(pluckthun)[IN] OR (nieba)[IN]	19	L1

END OF SEARCH HISTORY

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 NEWS  2  Jan 25  BLAST(R) searching in REGISTRY available in STN on the Web
 NEWS  3  Jan 29  FSTA has been reloaded and moves to weekly updates
 NEWS  4  Feb 01  DKILIT now produced by FIZ Karlsruhe and has a new update
                  frequency
 NEWS  5  Feb 19  Access via Tymnet and SprintNet Eliminated Effective 3/31/02
 NEWS  6  Mar 08  Gene Names now available in BIOSIS
 NEWS  7  Mar 22  TOXLIT no longer available
 NEWS  8  Mar 22  TRCTHERMO no longer available
 NEWS  9  Mar 28  US Provisional Priorities searched with P in CA/CAplus
                  and USPATFULL
 NEWS 10  Mar 28  LIPINSKI/CALC added for property searching in REGISTRY
 NEWS 11  Apr 02  PAPERCHEM no longer available on STN.  Use PAPERCHEM2 instead.
 NEWS 12  Apr 08  "Ask CAS" for self-help around the clock
 NEWS 13  Apr 09  BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS 14  Apr 09  ZDB will be removed from STN
 NEWS 15  Apr 19  US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
 NEWS 16  Apr 22  Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
 NEWS 17  Apr 22  BIOSIS Gene Names now available in TOXCENTER
 NEWS 18  Apr 22  Federal Research in Progress (FEDRIP) now available

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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FILE 'HOME' ENTERED AT 15:37:43 ON 30 MAY 2002

=> file medline caplus embase biosis
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                     0.21       0.21

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FILE 'BIOSIS' ENTERED AT 15:38:00 ON 30 MAY 2002
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=> s pluckthun A?/au or Nieba L?/au or honegger A?/au
L1          733 PLUCKTHUN A?/AU OR NIEBA L?/AU OR HONEGGER A?/AU

=> s l1 and antibod?
L2          355 L1 AND ANTIBOD?

=> s l2 and hydrophilic
L3            2 L2 AND HYDROPHILIC

=> s l2 and interface
L4           29 L2 AND INTERFACE

=> s l3 and l4
L5            2 L3 AND L4

=> s l3 or l4
L6           29 L3 OR L4

=> dis l5 1-2 ibib abs

L5   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         1999:449739  CAPLUS
DOCUMENT NUMBER:          132:90223
TITLE:                    SPM for functional identification of individual
                          biomolecules
AUTHOR(S):                Ros, Robert; Schwesinger, Falk; Padeste, Celestino;
                          Pluckthun, Andreas; Anselmetti, Dario;
                          Guentherodt, Hans-Joachim; Tiefenauer, Louis
CORPORATE SOURCE:         Molecular Nanotechnology, Paul Scherrer Institute,
                          Villigen, Switz.
SOURCE:                   Proceedings of SPIE-The International Society for
                          Optical Engineering (1999), 3607(Scanning and Force
                          Microscopies for Biomedical Applications), 84-89
                          CODEN: PSISDG; ISSN: 0277-786X
PUBLISHER:                SPIE-The International Society for Optical Engineering
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
```

AB The identification of specific binding mols. is of increasing interest in the context of drug development based on combinatorial libraries. Scanning Probe Microscopy (SPM) is the method of choice to image and probe individual biomols. on a surface. Functional identification of biomols. is a first step towards screening on a single mol. level. As a model system we use recombinant single-chain Fv fragment (scFv) **antibody** mols. directed against the antigen fluorescein. The scFv's are covalently immobilized on a flat gold surface via the C-terminal cysteine, resulting in a high accessibility of the binding site. The antigen is immobilized covalently via a long **hydrophilic** spacer to the silicon nitride SPM-tip. This arrangement allows a direct measurement of binding forces. Thus, closely related **antibody** mols. differing in only one amino acid at their binding site could be distinguished. A novel SPM-software has been developed which combines imaging, force spectroscopic modes, and online anal. This is a major prerequisite for future screening methods.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:71159 CAPLUS
DOCUMENT NUMBER: 128:139760
TITLE: Immunoglobulin superfamily domains and fragments with increased solubility
INVENTOR(S): **Pluckthun, Andreas; Nieba, Lars; Honegger, Annemarie**
PATENT ASSIGNEE(S): Morphosys Gesellschaft Fur Proteinoptimierung M.b.H., Germany; Pluckthun, Andreas; Nieba, Lars; Honegger, Annemarie
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9802462	A1	19980122	WO 1997-EP3792	19970716
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 938506	A1	19990901	EP 1997-934467	19970716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000516452	T2	20001212	JP 1998-505618	19970716

PRIORITY APPLN. INFO.: EP 1996-111441 A 19960716
WO 1997-EP3792 W 19970716

AB The present invention relates to the modification of Ig superfamily (IgSF) domains, IgSF fragments and fusion proteins thereof, esp. to the modification of **antibody** derivs., so as to improve their soly., and hence the yield, and ease of handling. The inventors have found that this can be achieved by making the region which comprises the **interface** with domains adjoined to said IgSF domain in a larger fragment or a full IgSF protein, and which becomes exposed in the IgSF domain, more **hydrophilic** by modification. The present invention describes DNA sequences encoding modified IgSF domains or fragments and fusion proteins thereof, vectors and hosts contg. these DNA sequences, IgSF domains or fragments or fusion proteins obtainable by expressing said DNA sequences in suitable expression systems, and a method for modifying IgSF domains, so as to improve their soly., expressibility and ease of handling.

=> dis his

(FILE 'HOME' ENTERED AT 15:37:43 ON 30 MAY 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 15:38:00 ON 30 MAY 2002
L1 733 S PLUCKTHUN A?/AU OR NIEBA L?/AU OR HONEGGER A?/AU
L2 355 S L1 AND ANTIBOD?
L3 2 S L2 AND HYDROPHILIC
L4 29 S L2 AND INTERFACE
L5 2 S L3 AND L4
L6 29 S L3 OR L4

=> s l4 and solubil9
9 IS NOT A RECOGNIZED COMMAND
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For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l4 and solubil?
L7 7 L4 AND SOLUBIL?

=> s l7 not l5
L8 6 L7 NOT L5

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9 3 DUP REM L8 (3 DUPLICATES REMOVED)

=> dis l9 1-3 ibib abs

L9 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2002:254315 BIOSIS
DOCUMENT NUMBER: PREV200200254315
TITLE: Biophysical properties of camelid VHH domains compared to those of human VH3 domains.
AUTHOR(S): Ewert, Stefan; Cambillau, Christian; Conrath, Katja; **Pluckthun, Andreas (1)**
CORPORATE SOURCE: (1) Biochemisches Institut, Universitat Zurich, Winterthurerstrasse 190, CH-8057, Zurich: plueckthun@biocfebs.unizh.ch Switzerland
SOURCE: Biochemistry, (March 19, 2002) Vol. 41, No. 11, pp. 3628-3636. http://pubs.acs.org/journals/bichaw/. print. ISSN: 0006-2960.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Camelidae possess an unusual form of **antibodies** lacking the light chains. The variable domain of these heavy chain **antibodies** (VHH) is not paired, while the VH domain of all other **antibodies** forms a heterodimer with the variable domain of the light chain (VL), held together by a hydrophobic **interface**. Here, we analyzed the

biophysical properties of four camelid VHH fragments (H14, AMD9, RN05, and CA05) and two human consensus VH3 domains with different CDR3 loops to gain insight into factors determining stability and aggregation of immunoglobulin domains. We show by denaturant-induced unfolding equilibria that the free energies of unfolding of VHH fragments are characterized by DELTAGN-U values between 21.1 and 35.0 kJ/mol and thus lie in the upper range of values for VH fragments from murine and human **antibodies** . Nevertheless, the VHH fragments studied here did not reach the high values between 39.7 and 52.7 kJ/mol of the human consensus VH3 domains with which they share the highest degree of sequence similarity. Temperature-induced unfolding of the VHH fragments that were studied proved to be reversible, and the binding affinity after cooling was fully retained. The melting temperatures were determined to be between 60.1 and 66.7 degreeC. In contrast, the studied VH3 domains aggregated during temperature-induced denaturation at 63-65 degreeC. In summary, the camelid VHH fragments are characterized by a favorable but not unusually high stability. Their hallmark is the ability to reversibly melt without aggregation, probably mediated by the surface mutations characterizing the VHH domains, which allow them to regain binding activity after heat renaturation.

L9 ANSWER 2 OF 3 MEDLINE
ACCESSION NUMBER: 1999321993 MEDLINE
DOCUMENT NUMBER: 99321993 PubMed ID: 10390351
TITLE: Removal of the conserved disulfide bridges from the scFv fragment of an **antibody**: effects on folding kinetics and aggregation.
AUTHOR: Ramm K; Gehrig P; **Pluckthun A**
CORPORATE SOURCE: Biochemisches Institut, Universitat Zurich, Winterthurerstr. 190, Zurich, CH-8057, Switzerland.
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (1999 Jul 9) 290 (2) 535-46. Journal code: J6V; 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990816
Last Updated on STN: 19990816
Entered Medline: 19990730

AB Fluorescence measurements and H/2H exchange experiments monitored by mass spectrometry have been applied to investigate the influence of the conserved disulfide bridges on the folding behavior and in vitro aggregation properties of the scFv fragment of the **antibody** hu4D5-8. A set of four proteins, carrying none, one, or both of the disulfide bridges have been compared regarding their stabilities, folding kinetics and tendency to aggregate. The results show that refolding of all four scFvs is ultimately limited by a slow proline isomerization in the VLdomain, since the native cis -conformation of proline L95 seems to be a prerequisite for formation of the native **interface**. Starting from short-term denatured protein, with the proline residues in their native conformation, a kinetically trapped intermediate is populated depending on the conditions, whose rate of conversion is slower than that of the fast-folding molecules. According to deuteron protection patterns determined by mass spectrometry, those domains retaining the disulfide bridge are able to form stable native-like structure, independent of native **interface** formation. The disulfide-free domains, in contrast, require the native **interface** for sufficient stabilization. The resistance of the scFvs towards aggregation seems to be critically dependent on the presence of the disulfide bridge in the VHdomain, and thus on the ability of the VHdomain to form stable structure prior to interaction with the VLdomain. The presence of a stable VLdomain in combination with a disulfide-free VHdomain appears to further promote aggregation, indicating the involvement of structured domains in the aggregates.

L9 ANSWER 3 OF 3 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 97337429 MEDLINE
DOCUMENT NUMBER: 97337429 PubMed ID: 9194169
TITLE: Disrupting the hydrophobic patches at the **antibody** variable/constant domain **interface**: improved in vivo folding and physical characterization of an engineered scFv fragment.
AUTHOR: **Nieba L**; **Honegger A**; Krebber C; **Pluckthun A**
CORPORATE SOURCE: Biochemisches Institut, Universitat Zurich, Switzerland.
SOURCE: PROTEIN ENGINEERING, (1997 Apr) 10 (4) 435-44. Journal code: PR1; 8801484. ISSN: 0269-2139.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199708
ENTRY DATE: Entered STN: 19970902
Last Updated on STN: 19970902
Entered Medline: 19970818

AB By constructing Fv and single-chain Fv (scFv) fragments of **antibodies**, the variable domains are taken out of their natural context in the Fab fragment, where they are associated with the constant domains of the light (CL) and heavy chain (CH1). As a consequence, all residues of the former variable/constant domain **interface** become solvent exposed. In an analysis of 30 non-redundant Fab structures it was found that at the former variable/constant domain **interface** of the Fv fragment the frequency of exposed hydrophobic residues is much higher than in the rest of the Fv fragment surface. We investigated the importance of these residues for different properties such as folding in vivo and in vitro, thermodynamic stability, **solubility** of the native protein and antigen affinity. The experimental model system was the scFv fragment of the anti-fluorescein **antibody** 4-4-20, of which only 2% is native when expressed in the periplasm of Escherichia coli. To improve its in vivo folding, a mutagenesis study of three newly exposed interfacial residues in various combinations was carried out. The replacement of one of the residues (V84D in VH) led to a 25-fold increase of the functional periplasmic expression yield of the scFv fragment of the **antibody** 4-4-20. With the purified scFv fragment it was shown that the thermodynamic stability and the antigen binding constant are not influenced by these mutations, but the rate of the thermally induced aggregation reaction is decreased. Only a minor effect on the **solubility** of the native protein was observed, demonstrating that the mutations prevent aggregation during folding and not of the native protein. Since the construction of all scFv fragments leads to the

exposure of these residues at the former variable/constant domain **interface**, this strategy should be generally applicable for improving the in vivo folding of scFv fragments and, by analogy, also the in vivo folding of other engineered protein domains.

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(FILE 'HOME' ENTERED AT 15:37:43 ON 30 MAY 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 15:38:00 ON 30 MAY 2002
L1 733 S PLUCKTHUN A?/AU OR NIEBA L?/AU OR HONEGGER A?/AU
L2 355 S L1 AND ANTIBOD?
L3 2 S L2 AND HYDROPHILIC
L4 29 S L2 AND INTERFACE
L5 2 S L3 AND L4
L6 29 S L3 OR L4
L7 7 S L4 AND SOLUBIL?
L8 6 S L7 NOT L5
L9 3 DUP REM L8 (3 DUPLICATES REMOVED)

=> s antibod? (P) hydroph? (P) interface? (P) solub?
L10 28 ANTIBOD? (P) HYDROPH? (P) INTERFACE? (P) SOLUB?

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11 11 DUP REM L10 (17 DUPLICATES REMOVED)

=> s l11 not l6
L12 9 L11 NOT L6

=> dis l12 1-9 ibib abs

L12 ANSWER 1 OF 9 MEDLINE
ACCESSION NUMBER: 2001088133 MEDLINE
DOCUMENT NUMBER: 20563850 PubMed ID: 11112523
TITLE: Estimation of the hydrophobic effect in an antigen-antibody protein-protein interface.
AUTHOR: Sundberg E J; Urrutia M; Braden B C; Isern J; Tsuchiya D; Fields B A; Malchiodi E L; Tormo J; Schwarz F P; Mariuzza R A
CORPORATE SOURCE: Center for Advanced Research in Biotechnology, University of Maryland Biotechnology Institute and National Institute of Standards and Technology, 9600 Gudelsky Drive, Rockville, Maryland 20850, USA.
CONTRACT NUMBER: GM52801 (NIGMS)
SOURCE: BIOCHEMISTRY, (2000 Dec 19) 39 (50) 15375-87.
Journal code: A0G. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1G7H; PDB-1G7I; PDB-1G7J; PDB-1G7L; PDB-1G7M
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010116

AB Antigen-**antibody** complexes provide useful models for analyzing the thermodynamics of protein-protein association reactions. We have employed site-directed mutagenesis, X-ray crystallography, and isothermal titration calorimetry to investigate the role of **hydrophobic** interactions in stabilizing the complex between the Fv fragment of the anti-hen egg white lysozyme (HEL) **antibody** D1.3 and HEL. Crystal structures of six FvD1.3-HEL mutant complexes in which an **interface** tryptophan residue (V(L)W92) has been replaced by residues with smaller side chains (alanine, serine, valine, aspartate, histidine, and phenylalanine) were determined to resolutions between 1.75 and 2.00 A. In the wild-type complex, V(L)W92 occupies a large **hydrophobic** pocket on the surface of HEL and constitutes an energetic "hot spot" for antigen binding. The losses in apolar buried surface area in the mutant complexes, relative to wild-type, range from 25 (V(L)F92) to 115 A(2) (V(L)A92), with no significant shifts in the positions of protein atoms at the mutation site for any of the complexes except V(L)A92, where there is a peptide flip. The affinities of the mutant Fv fragments for HEL are 10-100-fold lower than that of the original **antibody**. Formation of all six mutant complexes is marked by a decrease in binding enthalpy that exceeds the decrease in binding free energy, such that the loss in enthalpy is partly offset by a compensating gain in entropy. No correlation was observed between decreases in apolar, polar, or aggregate (sum of the apolar and polar) buried surface area in the V(L)92 mutant series and changes in the enthalpy of formation. Conversely, there exist linear correlations between losses of apolar buried surface and decreases in binding free energy (R(2) = 0.937) as well as increases in the solvent portion of the entropy of binding (R(2) = 0.909). The correlation between binding free energy and apolar buried surface area corresponds to 21 cal mol(-1) A(-2) (1 cal = 4.185 J) for the effective **hydrophobicity** at the V(L)92 mutation site. Furthermore, the slope of the line defined by the correlation between changes in binding free energy and solvent entropy approaches unity, demonstrating that the exclusion of solvent from the binding **interface** is the predominant energetic factor in the formation of this protein complex. Our estimate of the **hydrophobic** contribution to binding at site V(L)92 in the D1.3-HEL **interface** is consistent with values for the **hydrophobic** effect derived from classical hydrocarbon **solubility** models. We also show how residue V(L)W92 can contribute significantly less to stabilization when buried in a more polar pocket, illustrating the dependence of the **hydrophobic** effect on local environment at different sites in a protein-protein **interface**.

L12 ANSWER 2 OF 9 MEDLINE
ACCESSION NUMBER: 1998060757 MEDLINE
DOCUMENT NUMBER: 98060757 PubMed ID: 9398232
TITLE: Site-directed spin-labeling of transmembrane domain VII and the 4B1 antibody epitope in the lactose permease of Escherichia coli.
AUTHOR: Voss J; Hubbell W L; Hernandez-Borrell J; Kaback H R
CORPORATE SOURCE: Howard Hughes Medical Institute, Department of Physiology, University of California, Los Angeles, California 90095-1662, USA.
CONTRACT NUMBER: DK51131 (NIDDK)
EY05216 (NEI)

SOURCE: BIOCHEMISTRY, (1997 Dec 9) 36 (49) 15055-61.
Journal code: A0G; 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980122
Last Updated on STN: 19980122
Entered Medline: 19980106

AB Functional lactose permease mutants containing single Cys residues at positions 233-255 and a biotin acceptor domain at the C terminus were **solubilized** in dodecyl beta-d-maltopyranoside and purified by avidin affinity chromatography. Each mutant protein was derivatized with a thiol-selective nitroxide reagent and examined by conventional and power saturation electron paramagnetic resonance spectroscopy (EPR). The EPR spectral line shapes and the influence of nonpolar O2 or polar potassium chromium oxalate relaxation agents on the saturation behavior of the spin-labeled proteins were measured in order to obtain information on the mobility of the spin-labeled side chains and their accessibility to the relaxation agents, respectively. The results provide evidence that residues Ser233-Asn246 are within the **hydrophobic** core of the membrane and that Phe247 is at the lipid headgroup-solvent **interface**. Along with Phe247, Phe250 and Gly254 are also surface-exposed, as indicated by studies on the epitope for monoclonal **antibody** 4B1 [Sun, J., Wu, J., Carasco, N., and Kaback, H. R. (1996) Biochemistry 35, 990-998]. Furthermore, the nitroxide-labeled intramembrane Cys replacements exhibit variations in mobility and accessibility that are consistent with the conclusion that TM VII is an alpha-helix in contact with surrounding helices in the tertiary structure of the permease.

L12 ANSWER 3 OF 9 MEDLINE
ACCESSION NUMBER: 96061071 MEDLINE
DOCUMENT NUMBER: 96061071 PubMed ID: 7576085
TITLE: Solution properties of Escherichia coli-expressed VH domain of anti-neuraminidase antibody NC41.
AUTHOR: Kortt A A; Guthrie R E; Hinds M G; Power B E; Ivancic N; Caldwell J B; Gruen L C; Norton R S; Hudson P J
CORPORATE SOURCE: CSIRO, Division of Biomolecular Engineering, Parkville, Victoria, Australia.
SOURCE: JOURNAL OF PROTEIN CHEMISTRY, (1995 Apr) 14 (3) 167-78.
Journal code: AEJ; 8217321. ISSN: 0277-8033.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 19960124
Entered Medline: 19951128

AB The VH domain of anti-influenza neuraminidase **antibody** NC41, with and without a C-terminal **hydrophilic** marker peptide (FLAG), has been expressed in high yield (15-27 mg/L) in Escherichia coli. Both forms were secreted into the periplasm where they formed insoluble aggregates which were **solubilized** quantitatively with 2 M guanidine hydrochloride and purified to homogeneity by ion-exchange chromatography. The VH-FLAG was composed of three isoforms (pI values of approximately 4.6, 4.9, and 5.3) and the VH molecule was composed of two isoforms with pI values of 5.1 and 6.7; the difference between the VH isoforms was shown to be due to cyclization of the N-terminal glutamine residue in the pI 5.1 isoform. At 20 degrees C and concentrations of 5-10 mg/ml the VH domain dimerized in solution and then partly precipitated, resulting in the broadening of resonances in its 1H NMR spectrum. Reagents such as CHAPS, n-ocytylglucoside, and ethylene glycol, which presumably mask the exposed **hydrophobic interface** of the VH molecule, prevented dimerization of the VH and permitted good-quality NMR spectra on isotope-labeled protein to be obtained.

L12 ANSWER 4 OF 9 MEDLINE
ACCESSION NUMBER: 91330920 MEDLINE
DOCUMENT NUMBER: 91330920 PubMed ID: 1714390
TITLE: Localization on the mitochondrial F1 ATPase alpha subunit of an epitope masked in the membrane-bound enzyme using a monoclonal antibody and synthetic peptides.
AUTHOR: Moradi-Ameli M; Clerc F F; Cieur F; Seiberras G; Godinot C
CORPORATE SOURCE: Laboratoire de Biologie et Technologie des Membranes du CNRS, Villeurbanne, France.
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1991 Aug 1) 199 (3) 671-6.
Journal code: EMZ; 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: SWISSPROT-P80021
ENTRY MONTH: 199109
ENTRY DATE: Entered STN: 19911006
Last Updated on STN: 19960129
Entered Medline: 19910913

AB The epitope of the monoclonal **antibody** 20D6 was localized by N-terminal sequencing of the smallest immunoreactive peptides obtained after CNBr and trypsin cleavage of the F1 alpha subunit of the mitochondrial ATPase/ATP synthase. Immunochemical analysis of overlapping synthetic octapeptides, covering the immunoreactive peptide sequence, has defined the seven-amino-acid sequence recognized by 20D6 as 84EGDIVKR90. The binding of 20D6 was lost after substituting either I87 by K or S, or R90 by C or A as it occurs in the alpha subunit sequence of Escherichia coli or chloroplast ATPase, respectively. This explained the lack of immunoreactivity of 20D6 to these species and indicated the importance of charged as well as **hydrophobic** residues in the epitope. Immunochemical analysis of synthetic peptides by polyclonal anti-F1 antisera showed that this region is highly immunodominant. In a competitive ELISA, the monoclonal **antibody** bound with similar affinity to F1 in the presence and absence of substrate as well as to cold dissociated F1, indicating that the epitope was located on the surface of the alpha subunit and not buried between F1 subunits. The lack of binding of 20D6 when F1 is bound to the membrane showed that the epitope exposed at the surface of purified **soluble** F1 became masked after binding to the membrane. This suggests that it is located at the **interface** between F1 and the membrane.

L12 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:949582 CAPLUS
DOCUMENT NUMBER: 123:333275
TITLE: Hydrophobicity of biosurfaces - origin, quantitative determination and interaction energies
AUTHOR(S): van Oss, C. J.
CORPORATE SOURCE: Departments of Microbiology and Chemical Engineering, State University of New York at Buffalo, Buffalo, NY, 14214-3078, USA
SOURCE: Colloids Surf., B (1995), 5(3/4), 91-110
CODEN: CSBBEQ; ISSN: 0927-7765
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It is shown that the "**hydrophobic**" attraction energy between two apolar moieties (as well as between one polar and one apolar moiety) immersed in water is the sole consequence of the hydrogen-bonding energy of cohesion of the water mols. surrounding these moieties. It is also shown that "**hydrophobic**" surfaces do not repel, but on the contrary attract water. The theory is given of **hydrophobic** interactions at a macroscopic level, as well as various methods for their quant. measurement. The properties of **hydrophobic**, partly **hydrophobic** and **hydrophilic** compds. and surfaces are described, including those of amino acids, proteins (incorporating protein **soly**.), proteins at the air-water **interface**, carbohydrates, phospholipids, phospholipid layers, and nucleic acids. Finally, some effects and applications of **hydrophobic** interactions are discussed, including protein adsorption, protein pptn., cell adhesion, cell fusion, and liq. chromatog. approaches such as reversed-phase and **hydrophobic** interaction chromatog. Finally, the influence of **hydrophobic** forces is treated in antigen-**antibody** and other ligand-receptor interactions.

L12 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:79875 CAPLUS
DOCUMENT NUMBER: 116:79875
TITLE: Process and apparatus for separation by carrier-mediated transport
INVENTOR(S): Cohen, Charles M.; Dishman, Robert A.; Huston, James S.; Bratzler, Robert L.; Dodds, David R.; Zepp, Charles M.
PATENT ASSIGNEE(S): Creative Biomolecules, Inc., USA; Sepracor, Inc.
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9112072	A1	19910822	WO 1991-US627	19910130
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
US 5167824	A	19921201	US 1990-479935	19900214
AU 9172491	A1	19910903	AU 1991-72491	19910130
AU 637884	B2	19930610		
EP 516686	A1	19921209	EP 1991-904736	19910130
EP 516686	B1	19960313		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05504094	T2	19930701	JP 1991-504476	19910130
AT 135257	E	19960315	AT 1991-904736	19910130

PRIORITY APPLN. INFO.: US 1990-479935 19900214
WO 1991-US627 19910130

AB Disclosed are processes and app. for sepg. a desired solute, such as an optically active isomer, from a complex mixt. using carrier-facilitated transport in an immobilized liq. membrane or carrier-facilitated solvent extn. The carrier is a binding protein selected and/or engineered to immunochem. reversibly bind to the solute and to have a significant **soly**. in the extg. solvent or immobilized liq. membrane. The app. comprises (a) a 1st membrane; (b) a **hydrophilic** liq. phase in contact with the membrane; (c) means for passing a **hydrophobic** feed soln. into contact with the membrane **interface**, the feed soln. contg. the desired solute in a solvent immiscible with the **hydrophilic** phase; and (d) a binding protein dissolved in the **hydrophilic** phase for immunochem. binding the solute at the membrane **interface**. Various app. and process embodiments are described and diagrammed. A genetically-engineered single-chain fusion protein, comprising the heavy- and light-chain variable region binding sites of a monoclonal **antibody** to digoxin, was prepd. and used to ext. oleandrin in a supported liq. membrane process. Resoln. of naproxen is also described.

L12 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1972:55278 CAPLUS
DOCUMENT NUMBER: 76:55278
TITLE: Water surface free energy and its potential in biochemical activities
AUTHOR(S): Lewin, S.
CORPORATE SOURCE: Dep. Postgrad. Mol. Biol., N. East London Polytech., London, Engl.
SOURCE: Biochem. J. (1971), 124(5), 67P-68P
CODEN: BIJOAK
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A brief discussion of how the presence of **hydrophobic** groups in **sol**. biochem. entities, such as proteins, results in the formation of water-**hydrophobic** group **interfaces** to which **interface** free-energy and entropy considerations apply. Lowering the surface tension of solns. can reverse antigen-**antibody** complex formation, disaggregate tobacco mosaic virus, and decrease the equil. const. of human serum. The contribution of high urea and high guanidinium chloride concns. to lowering **interface** tension, and therefore to deadherence of **hydrophobic** groups, should be taken into account in considering helix-coil transformations. 6 refs.

L12 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1968:101861 CAPLUS
DOCUMENT NUMBER: 68:101861
TITLE: Interaction of soluble proteins with protein monolayers
AUTHOR(S): Arnold, John D.; Pak, Charles Y. C.
CORPORATE SOURCE: Kansas City Gen. Hosp., Kansas City, Mo., USA

SOURCE: J. Am. Oil Chem. Soc. (1968), 45(3), 128-38
CODEN: JAOCA7
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The direction and strength of intermol. forces at an air-H2O or oil-H2O **interface** is such that many proteins in the **interface** are distorted in structure. This involves changes in **soly.** and cross-sectional area. Many of the changes can be accounted for by rupture of the secondary and tertiary bonds and are often irreversible. The **hydrophilic** groups of the protein will be concd. in the aq. phase and participate in interactions with normal proteins in the supporting soln. Certain types of interaction between these **hydrophilic** groups of a protein monofilm and a **sol.** protein are dependent on the interfacial pressure, which is sensitive to small (1 or more amino acid) changes in structure of the protein. Evidence is given that they are related to certain antigen-**antibody** type reactions between mols. in 3-dimensional systems. Since many proteins in vivo are exposed to oil-H2O and air-H2O **interfaces**, this lab. model may have physiologic as well as chem. significance.

L12 ANSWER 9 OF 9 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95193634 EMBASE
DOCUMENT NUMBER: 1995193634
TITLE: Biophysical view of the role of interfaces in biomolecular recognition.
AUTHOR: Cevc G.
CORPORATE SOURCE: Medizinische Biophysik, Technische Universitat Munchen, Klinikum r.d.l., Ismaningerstr. 22,D-81675 Munchen, E.U., Germany
SOURCE: Biophysical Chemistry, (1995) 55/1-2 (43-53).
ISSN: 0301-4622 CODEN: BICIAZ
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Molecular recognition plays a key role in life. Macromolecular interactions at and with **interfaces** are of paramount importance in this respect. It is therefore crucial to understand and quantify the forces near the surfaces of biological interest in sufficient detail. Specific binding of large molecules, such as **antibodies**, is affected by the proximity of polar surfaces, for example. On the one hand, the presence of the net surface charges may raise or lower the local macromolecular concentration depending on the relative sign of the charges involved. On the other hand, the ligands attached to strongly polar surfaces always attract and bind their corresponding **antibodies** less efficiently than the corresponding dissolved molecules. The reason for this is the non-Coulombic repulsion between the ligand-presenting polar surface and the approaching macromolecule. This force is promoted by the surface **hydrophilicity** and the width of the interfacial region. A simple, direct hydration force is seldom, if ever, seen in such systems. (This is owing to the very short range (A(h) .simeq. 0.1 nm) of pure hydration force.) The non-specific adsorption of proteins to the lipid bilayer is also little affected by the overall repulsion between the macromolecule and the bilayer surface; such an adsorption is governed more by the number of defects and/or by the availability of the **hydrophobic** binding sites in the interfacial region. Artificial lipid membranes typically offer numerous such binding sites to the surrounding macromolecules. Multiple non- specific protein adsorption, which results in partial macromolecular denaturation or complement activation, is therefore one of the main reasons for the rapid elimination of lipid vesicles from the blood stream in vivo. To promote the circulation time of an intravenously injected lipid suspension it is therefore necessary to modify the surfaces of their constituent lipid bilayers. Increasing the surface net charge density and/or increasing the bilayer surface **hydrophilicity** is of little use in this respect. In order to affect the non-specific bilayer-protein interactions significantly, an optimal number of water-**soluble**, short and sufficiently mobile polymers must be attached to the lipid head-groups. These polymers then increase the repulsive barrier of the membrane surface dramatically, due to the generation of a thick and mobile as well as strongly hydrated **interface**. Owing to this, the affinity for proteins of the resulting surface is lowered and the surface-induced protein denaturation or complement insertion is hampered. Polymer-coated liposomes, consequently, are not attractive for the phagocytic cells. Such liposomes, consequently, remain in the blood circulation much longer than simple lipid vesicles; the former, consequently, may spontaneously accumulate in tumors.

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(FILE 'HOME' ENTERED AT 15:37:43 ON 30 MAY 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 15:38:00 ON 30 MAY 2002
L1 733 S PLUCKTHUN A?/AU OR NIEBA L?/AU OR HONEGGER A?/AU
L2 355 S L1 AND ANTIBOD?
L3 2 S L2 AND HYDROPHILIC
L4 29 S L2 AND INTERFACE
L5 2 S L3 AND L4
L6 29 S L3 OR L4
L7 7 S L4 AND SOLUBIL?
L8 6 S L7 NOT L5
L9 3 DUP REM L8 (3 DUPLICATES REMOVED)
L10 28 S ANTIBOD? (P) HYDROPH? (P) INTERFACE? (P) SOLUB?
L11 11 DUP REM L10 (17 DUPLICATES REMOVED)
L12 9 S L11 NOT L6

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